REMARKS

Applicants request reconsideration on the merits of the above-referenced patent application.

I. Amendments to the Specification

In accordance with MPEP §608.01(v)(I), Applicants have amended the specification to capitalize "TENOX 8" everywhere it appears, and have marked it with a superscripted "®."

Applicants have amended the discussion relating to US Patent 6,387,381 to be more consistent with, for example, lines 20-21 of col. 4 in US Patent 6,387,381.

Applicants have amended the specification to include a generic definition for TENOX® 8. This generic definition is from the revised MSDS for TENOX® 8 **(enclosed)**. Given that the date for the revised MSDS is May 13, 2003, Applicants submit that the generic definition was known before the August 13, 2003 filing date of Applicants' parent PCT application.

II. Amendments to the Claims

This amendment adds claims 19-22. Thus, claims 1-5, 7-10, and 12-22 are pending. Claims 9, 10, and 12-17 are withdrawn. Accordingly, claims 1-5. 7, 8, and 18-22 are under consideration. This amendment amends claims 1, 8, 9, 12-15, 17, and 18. Applicants submit that these amendments and new claims do not introduce new matter:

Claim 1 has been amended to more specifically define the first additive as ivermectin. This amendment is supported by Applicants' specification at, for example, page 13, line 17 to page 14, line 12; page 18, lines 17-21; and Examples 1b and 2 on pages 22-24.

Claim 1 has been amended to define the moisture content as being less than about 15%. This amendment is supported by Applicants' specification at, for example, page 13, lines 12-13; and claim 1 as originally filed.

Claim 1 has been rephrased to characterize the formulation as comprising a knockout formulation. This amendment is permissible under MPEP §2163.07.

Claim 8 has been amended to further define the second additive of claim 4 rather than the first additive of claim 1. This amendment is supported by Applicants' specification at, for example, page 13, line 17 to page 14, line 20.

Claims 9, 12, 14, and 15 have been amended to define the additive as ivermectin. These amendments are supported by Applicants' specification at, for example, page 13, line 17 to page 14, line 12; page 18, lines 17-21; and Examples 1b and 2 on pages 22-24.

Claim 13 has been amended to remove a redundant "the." This amendment is permissible under MPEP §2163.07.

Claim 17 has been amended to more clearly indicate that the composition may comprise one or more than one additional additive, as well as to more specifically define the additional additive(s). This amendment is supported by Applicants' specification at, for example, page 13, line 17 to page 14, line 20.

Claim 18 has been amended to be independent. Accordingly, claim 18 has been amended to also incorporate the provision that the formulation comprise a knockout formulation and not an extrudate. This amendment is supported by Applicants' specification at, for example, the paragraph bridging lines 9-16 on page 17; and Example 1b on pages 22-23.

Claim 18 has been amended to remove the term "about" to be more consistent with Example 1b on page 22.

Claim 18 has been amended to remove the unnecessary statements characterizing the concentrations as being based on total try weight of the formulation.

Claim 18 has been amended to remove the requirement that the formulation comprise an antioxidant.

New claim 19 is supported by Applicants' specification at, for example, page 14, lines 4-6.

New claim 20 is supported by Applicants' specification at, for example, page 13, line 17 to page 14, line 20.

New claim 21 is supported by Applicants' specification at, for example, page 14, lines 4-7; and page 24, lines 9-19

New claim 22 is supported by Applicants' specification at, for example, page 13, lines 12-13; and Examples 1a, 1b, and 2 on pages 19-25.

Applicants reserve the right to pursue any canceled or other subject matter disclosed in this application in one or more divisional and/or continuation applications.

III. Response to opening comments

The opening comments on page 2 of the Office action indicate that only claims 1-5, 7, and 8 are under consideration. However, the Office action summary on the previous page indicates that claim 18 is under consideration, as do the claim rejections. Thus, this amendment identifies claim 18 as being "previously presented" rather than "withdrawn."

IV. Response to acknowledgement of information disclosure statements

Applicants thank the Examiner for reviewing the February 20, 2005 and October 15, 2007 Information Disclosure Statements. Applicants respectfully request that the Examiner initial each citation on the Form PTO/SB/08a's, and then sign and date each Form PTO/SB/08a in accordance with MPEP §609 to ensure that all the references are cited on the face of the resulting patent. Applicants also request the Examiner to do the same with the Supplemental Information Disclosure Statement that Applicants are submitting in parallel with this Amendment.

V. Response to reminder relating to abstract

Applicants thank the Examiner for the reminder as to the content and form of the abstract. Applicants believe that the abstract complies with the Patent Office's rules. Thus, Applicants have not amended the abstract. If, however, the Examiner has any specific concerns regarding the abstract, Applicants request that the Examiner identify them.

VI. Response to the objection relating to the use of "Tenox 8"

An objection has been raised to the term TENOX 8. Specifically, the Office action indicates that the term TENOX 8 should be capitalized everywhere it is used, and that a generic definition for the term should be added to the specification. Applicants request withdrawal of this objection.

In accordance with MPEP §608.01(v)(I), Applicants have amended the specification to capitalize the term everywhere it appears, and have marked it with a superscripted "®." This capitalization and marking of TENOX 8 is not intended to be an admission by Applicants or the Assignee that TENOX 8 has been, is, or ever will be valid or enforceable.

As to the requirement that a generic definition be added to the specification, Applicants respectfully submit that the specification is not required to have a generic definition, given that the generic definition was known in the art before their parent PCT application was filed. After all, as noted in MPEP §2164.01, a patent "preferably omits" anything that is already well known in the art. Nevertheless, in an effort to expedite prosecution of this application, Applicants have amended the specification to include the generic definition provided by the May 13, 2003 revised MSDS for TENOX 8 **(enclosed)**. Applicants thank the Examiner for taking the initiative to search for a generic definition.

VII. Response to obviousness-type double patenting rejection

Claims 1, 7, and 8 have been provisionally rejected as being unpatentable over claims 2-5 of co-pending US Patent Appl. 11/100,982 (Publ. No. 2005/0226908) on the grounds of obviousness-type double patenting. Applicants request withdrawal of this rejection.

At the outset, Applicants note that, as of this filing, US Patent Appl. 11/100,982 has not issued, and, to the best of their knowledge, has not been allowed. Thus, regardless of the merits, this rejection is not ripe. Moreover, Applicants respectfully submit that there is no double-patenting issue. More specifically, claims 2-5 in US Patent Appl. 11/100,982 have been amended to depend directly or indirectly from claim 6 of that application. Claim 6 is directed to a treatment method:

> 6. A method for treating an organism against a *Toxocara canis, Ancylostoma caninum, Trichuris vulpis, Dipylidium caninum*, and/or *Dirofilaria immitis* infection, wherein:
>
> the method comprises administering a composition to the organism a single time;
>
> the composition comprises a benzimidazole, an avermectin, and praziquantel; and
>
> administration of the composition provides the following amounts of benzimidazole, avermectin, and praziquantel to the organism:
>
> from about 25 to about 500 mg fenbendazole per kg body weight,
>
> from about 0.002 to about 200 mg ivermectin per kg body weight, and
>
> from about 0.002 to about 200 mg praziquantel per kg body weight.

Claims 1, 7, and 8 of the instant application, in contrast, are directed to a pharmaceutical soft chew formulation. Thus, Applicants submit that claims 1, 7, and 8 are patentably distinct from claims 2-5 of US Patent Appl. 11/100,982.

For the Examiner's convenience, Applicants have **enclosed** all the claims from US Patent Appl. 11/100,982 (as they are pending as of this filing).

VIII. Response to written description rejection of claim 18 under 35 U.S.C. §112 (first paragraph)

Claim 18 has been rejected under 35 U.S.C. §112 (first paragraph) for failing to satisfy the written description requirement. More specifically, claim 18 has been rejected for using the term "about" to characterize the component concentrations. Applicants request withdrawal of this rejection. In an effort to expedite prosecution of this application, Applicants have amended claim 18 to remove the term "about." Applicants, however, make no representation with respect to the merits of this rejection.

IX. Response to enablement rejection of claim 18 under 35 U.S.C. §112 (first paragraph)

Claim 18 has been rejected under 35 U.S.C. §112 (first paragraph) for failing to satisfy the enablement requirement. More specifically, one of the components recited in claim 18 is an antioxidant. The Office action asserts that Applicants' specification is enabling only to a limited class of antioxidants (such as TENOX® 8) rather than the entire generic class of antioxidants. Applicants request withdrawal of this rejection. In an effort to expedite prosecution of this application, Applicants have amended claim 18 to remove the requirement for an antioxidant. Applicants, however, make no representation with respect to the merits of this rejection.

X. Response to indefiniteness rejection of claim 18 under 35 U.S.C. §112 (second paragraph)

Claim 18 has been rejected under 35 U.S.C. §112 (first paragraph) for being indefinite for failing to point out and distinctly claim the invention. More specifically, claim 18 has been rejected for not expressly identifying how the components recited in claim 18 relate to the more generic components recited in claim 1. Applicants request withdrawal of this rejection.

Applicants respectfully submit that claim 18 falls within the scope of claim 1, and, therefore, is a proper dependent claim. Applicants are not aware of any requirement that a dependent claim expressly correlate its components to those of a dominant claim. Nevertheless, in an effort to expedite prosecution of this patent application, Applicants have amended claim 18 to be independent. Thus, the rejection has been rendered moot.

XI. Response to obviousness rejection of claims 1-5, 7, 8, and 18 under 35 U.S.C. §103(a)

Claims 1-5, 8, 7, and 18 have been rejected under 35 U.S.C. §103(a) as being obvious over Christenen (US Patent Appl. Publ. 2001/0036464) in view of Monte (US Patent 5,578,336) and Miller (US Patent 5,439,924). Applicants request withdrawal of this rejection.

A. Claim 1

Claim 1 is directed to a pharmaceutical soft chew formulation that comprises a **knockout** formulation. Knockout formulations are generally different from, for example, extrudates or tablets formed with tablet presses. For example, extrudates or tablets formed with tablet presses generally are subjected to different types of pressures, shear stresses, and/or temperatures relative to knockout formulations. Such differences can affect the physical characteristics of the formulation or create inconsistencies from one batch to the next. Applicants' specification discusses some such potential effects with respect to tablets formed with tablet presses. *See, e.g.*, Applicants' specification, page 2, line 14 to page 3, line 15. And, with respect to extrudates, such potential effects are well known in the art. *See, e.g.*, US Patent Appl. Publ. 2008/0075759, paragraphs 7-9 **(enclosed)**.

To support a *prima facie* showing of obviousness, the prior art must teach or suggest all the claim limitations. *See* MPEP §2143. Applicants respectfully submit that this threshold has not been met. More specifically, **the cited references fail to teach, suggest, or provide motivation for a *knockout* formulation.** To the contrary, Christensen discusses extrudates. Christensen provides no instruction with respect to knockout formulations. And Monte and Miller fail to cure this deficiency. Monte, for example, discusses a tablet containing a chewy candy (or gum) center. This chewy candy (or gum) center is completely coated by at least two coatings. These coatings include an outer coating that contains an active ingredient, and an

intermediate coating that separates that outer coating from the chewy candy (or gum) center. Monte provides no indication that such tablets could comprise a knockout formulation. Miller, on the other hand, generically discusses chewable wafer or tablet dose forms, but fails to discuss any knockout formulations. In fact, Miller instead purports to illustrate tablets formed with tablet presses. *See, e.g.*, Miller, Col. 12, lines 42-44 and 66-68. Accordingly, for at least this reason, Applicants respectfully submit that this rejection should be withdrawn.

B. *Claims 2-5, 7-10, 12-17, and 19-22*

Claims 2-5, 7-10, and 12-17 (as well as new claims 19-22) depend directly or indirectly from claim 1, and, therefore, are patentable over the cited references for the same reasons as claim 1, as well as the additional limitations that they respectively recite.

New claim 22, in particular, is directed to a water-free knockout formulation. The cited references fail to teach, suggest, or provide motivation for such a formulation. To the contrary, Christensen discusses formulations that contain 5-20% water (*see, e.g.,* paragraph 6). Christensen does not discuss any water-free formulations. Monte and Miller fail to cure this deficiency. Monte, for example, discusses tablets having a chewy candy core containing 1-95% water (*see, e.g.*, col. 19, lines 50-51). And, while Miller does purport to illustrate a water-free tablet formulation, that formulation was prepared with a tablet press (*see, e.g.*, col. 12, lines 48-68). Moreover, such a water-free formulation cannot be used to modify the teachings of Christensen. Christensen, after all, focuses on a purported invention for adjusting the water activity in water-containing formulations. A water-free formulation obviously would defeat that purpose. *See* MPEP §2143.01 ("If proposed modification would render the prior art invention being modified unsatisfactory for its intended purpose, then there is no suggestion or motivation to make the proposed modification."). Thus, for at least this additional reason, claim 22 is patentable over the cited references.

C. *Claim 18*

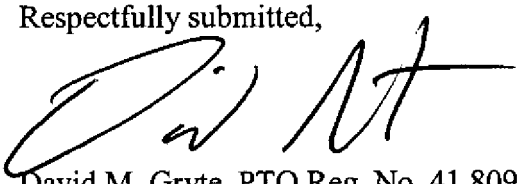
Claim 18, like claim 1, is directed to a pharmaceutical soft chew formulation that comprises a knockout formulation. Thus, claim 18 is patentable over the cited references for at least the reason discussed above with respect to claim 1.

* * * * * * * * *

Applicants do not believe that any fee is due in connection with this filing. If, however, any such fee(s) is due, the Commissioner is hereby authorized to charge the fee(s) to Deposit Account No. **02-2334**. In addition, if there is ever any other fee deficiency or overpayment under 37 C.F.R. §1.16 or 1.17 in connection with this patent application, the Commissioner is hereby authorized to charge such deficiency or overpayment to Deposit Account No. **02-2334**.

Applicants submit that this application is in condition for allowance, and request that the application be allowed. Applicants also request that the Examiner call the Undersigned if any issues arise that can be addressed over the phone to expedite examination of this application.

Respectfully submitted,



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DMG/DAP
enclosures

EASTMAN

MATERIAL SAFETY DATA SHEET

Revision Date: 05/13/2003
MSDSUSA/ANSI/EN/150000001359/Version 2.0

1. CHEMICAL PRODUCT AND COMPANY IDENTIFICATION

Product Name	Tenox(TM) 8 Food-Grade Antioxidant, Kosher
Product Identification Number(s)	01782-00, P0178200, P0178201, P0178202, P0178203, P0178204, P0178205, P0178207, P0178208, P0178209, P017820A, P017820B, P017820C, P017820D, P0178206
Manufacturer/Supplier	Eastman Chemical Company 200 South Wilcox Drive Kingsport, TN 37660-5280 US +14232292000
MSDS Prepared by	Eastman Product Safety and Health
Chemical Name	not applicable
Synonym(s)	023624
Molecular Formula	not applicable
Molecular Weight	not applicable
Product Use	antioxidant (food grade)
OSHA Status	hazardous

For emergency health, safety & environmental information, call 800-EASTMAN.

For emergency transportation information, call CHEMTREC at 800-424-9300 or call 800-EASTMAN.

2. COMPOSITION INFORMATION ON INGREDIENTS

(Typical composition is given, and it may vary. A certificate of analysis can be provided.)

Weight %	Component	CAS Registry No.
80%	corn oil	8001-30-7
20%	butylated hydroxytoluene	128-37-0

3. HAZARDS IDENTIFICATION

CAUTION!
AT ELEVATED TEMPERATURES, VAPOR MAY CAUSE IRRITATION OF EYES AND RESPIRATORY TRACT

HMIS® Hazard Ratings: Health - 1, Flammability -1, Chemical Reactivity - 0

HMIS® rating involves data interpretations that may vary from company to company. They are intended only for rapid, general identification of the magnitude of the specific hazard. To deal adequately with the safe handling of this material, all the information contained in this MSDS must be considered.

4. FIRST-AID MEASURES

Inhalation: If symptomatic, move to fresh air. Get medical attention if symptoms persist.
Eyes: Any material that contacts the eye should be washed out immediately with water. If easy to do, remove contact lenses. Get medical attention if symptoms persist.
Skin: Wash with soap and water. Get medical attention if symptoms occur.
Ingestion: Seek medical advice.

5. FIRE FIGHTING MEASURES

Extinguishing Media: water spray, dry chemical, carbon dioxide, foam
Special Fire-Fighting Procedures: Wear self-contained breathing apparatus and protective clothing. USE WATER WITH CAUTION. Material will float and may ignite on surface of water.
Hazardous Combustion Products: carbon dioxide, carbon monoxide

6. ACCIDENTAL RELEASE MEASURES

Use personal protective equipment. Absorb spill with vermiculite or other inert material, then place in a container for chemical waste.
For Large Spills: Flush spill area with water spray. Prevent runoff from entering drains, sewers, or streams.

7. HANDLING AND STORAGE

Personal Precautionary Measures: Avoid breathing vapor from heated material. Use only with adequate ventilation.
Prevention of Fire and Explosion: Keep from contact with oxidizing materials.
Storage: Keep container closed. This material may be used in food. Protect from contamination. Do not store or ship together with odorous substances, toxic substances.
Additional Information: Protect from freezing. Store between 10°C (50°F) and 32°C (90°F) to avoid separation and prolong shelf life.

8. EXPOSURE CONTROLS/PERSONAL PROTECTION

Country specific exposure limits have not been established or are not applicable unless listed below.

2,6-DI-TERT-BUTYL-P-CRESOL
US. NIOSH: Pocket Guide to Chemical Hazards
Recommended exposure limit (REL): 10 mg/m3
2,6-DITERT. BUTYL-P-CRESOL
US. OSHA Table Z-1-A (29 CFR 1910.1000)
Time Weighted Average (TWA): 10 mg/m3
BUTYLATED HYDROXYTOLUENE (BHT), VAPOR AND AEROSOL, INHALABLE FRACTION
US. ACGIH Threshold Limit Values

Time Weighted Average (TWA): 2 mg/m3

2,6-DITERT-BUTYL-P-CRESOL
US. California Code of Regulations, Title 8, Section 5155. Airborne Contaminants
Time Weighted Average (TWA) Permissible Exposure Limit (PEL): 10 mg/m3

BUTYLATED HYDROXYTOLUENE (BHT), VAPOR AND AEROSOL, INHALABLE FRACTION
US. ACGIH Threshold Limit Values
Listed.

2,6-DI-TERT-BUTYL-P-CRESOL
US. NIOSH: Pocket Guide to Chemical Hazards
Listed.

2,6-DITERT. BUTYL-P-CRESOL
US. OSHA Table Z-1-A (29 CFR 1910.1000)
Listed.

2,6-DITERT-BUTYL-P-CRESOL
US. California Code of Regulations, Title 8, Section 5155. Airborne Contaminants
Listed.

Ventilation: Good general ventilation (typically 10 air changes per hour) should be used. Ventilation rates should be matched to conditions. If applicable, use process enclosures, local exhaust ventilation, or other engineering controls to maintain airborne levels below recommended exposure limits. If exposure limits have not been established, maintain airborne levels to an acceptable level.

Respiratory Protection: If engineering controls do not maintain airborne concentrations below recommended exposure limits (where applicable) or to an acceptable level (in countries where exposure limits have not been established), an approved respirator must be worn. In the United States of America, if respirators are used, a program should be instituted to assure compliance with OSHA Standard 63 FR 1152, January 8, 1998. Respirator type: organic vapor

Eye Protection: It is a good industrial hygiene practice to minimize eye contact.

Skin Protection: It is a good industrial hygiene practice to minimize skin contact.

Recommended Decontamination Facilities: eye bath, washing facilities

9. PHYSICAL AND CHEMICAL PROPERTIES

Physical Form: liquid
Color: light yellow
Odor: slight
Specific Gravity: 0.925 (20 °C)
Boiling Point: > 204 °C
Solubility in Water: negligible
Flash Point: 139 °C (Pensky-Martens closed cup)
Thermal Decomposition Temperature: (DTA) No exotherm to 500° C

10. STABILITY AND REACTIVITY

Stability:	Stable.
Incompatibility:	Material reacts with strong oxidizing agents.
Hazardous Polymerization:	Will not occur.

11. TOXICOLOGICAL INFORMATION

Acute toxicity data, if available, are listed below. Additional toxicity data may be available on request.

12. ECOLOGICAL INFORMATION

Acute toxicity data, if available, are listed below. Additional toxicity data may be available on request.

This material has not been tested for environmental effects.

13. DISPOSAL CONSIDERATIONS

Discharge, treatment, or disposal may be subject to national, state, or local laws. Incinerate. Since emptied containers retain product residue, follow label warnings even after container is emptied.

14. TRANSPORT INFORMATION

Marine pollutant components: none unless listed below

DOT (USA): Class not regulated

ICAO Status: Class not regulated

IMDG Status: Class not regulated

15. REGULATORY INFORMATION

WHMIS (Canada) Status: noncontrolled

SARA 311-312 Hazard Classification(s):
immediate (acute) health hazard

SARA 313: none, unless listed below

Carcinogenicity Classification (components present at 0.1% or more): none, unless listed below

TSCA (US Toxic Substances Control Act): All components of this product are listed on the TSCA inventory. Any impurities present in this product are exempt from listing.

DSL (Canadian Domestic Substances List) and CEPA (Canadian Environmental Protection Act): All components of this product are listed on the DSL. Any impurities present in this product are exempt from listing.

EINECS (European Inventory of Existing Commercial Chemical Substances): All components of this product are listed on EINECS.

AICS / NICNAS (Australian Inventory of Chemical Substances and National Industrial Chemicals Notification and Assessment Scheme): All components of this product are listed on AICS or otherwise comply with NICNAS.

MITI (Japanese Handbook of Existing and New Chemical Substances): All components of this product are listed in the Handbook or have been approved in Japan by new substance notification.

ECL (Korean Toxic Substances Control Act): All components of this product are listed on the Korean inventory or otherwise comply with the Korean Toxic Substances Control Act.

16. OTHER INFORMATION

Visit our website at www.EASTMAN.com or call 001-423-229-2000.

The information contained herein is based on current knowledge and experience; no responsibility is accepted that the information is sufficient or correct in all cases. Users should consider these data only as a supplement to other information. Users should make independent determinations of suitability and completeness of information from all sources to assure proper use and disposal of these materials, the safety and health of employees and customers, and the protection of the environment.

Highlighted areas indicate new or changed information.

Pending Claims in US Appl. 11/100,982 as of August 6, 2008

Claim 1 (canceled).

2. The method of Claim 6, wherein:
the composition is in the form of a soft chew;
the soft chew comprises:
a flavoring component of between about 0.1 to about 50 percent,
a starch component of between about 5.0 to about 60 percent,
a sugar component of between about 5.0 to about 75 percent,
an oil component of between about 1.0 to about 40 percent, and
an additive;
the moisture content of the composition is less than about 15 percent;
the soft chew is formed by knockout; and
the soft chew is not an extrudate.

3. The method of Claim 2, wherein the additive is selected from the group consisting of a pharmaceutical, nutraceutical, vitamin, mineral, and filler.

4. The method of Claim 2, wherein the flavoring component is selected from the group consisting of fruit, meat, vegetable, cheese, cheese-bacon, artificial flavoring, and mixtures thereof.

5. A method of claim 6, wherein:
the benzimidazole comprises Fenbendazole, and
the avermectin comprises Ivermectin.

6. A method for treating an organism against a *Toxocara canis, Ancylostoma caninum, Trichuris vulpis, Dipylidium caninum*, and/or *Dirofilaria immitis* infection, wherein:
the method comprises administering a composition to the organism a single time;
the composition comprises a benzimidazole, an avermectin, and praziquantel; and

administration of the composition provides the following amounts of benzimidazole, avermectin, and praziquantel to the organism:

from about 25 to about 500 mg fenbendazole per kg body weight,

from about 0.002 to about 200 mg ivermectin per kg body weight, and

from about 0.002 to about 200 mg praziquantel per kg body weight.

Claim 7 (canceled).

8. The method of Claim 6, wherein the organism is a dog.

Claims 9-18 (canceled).

19. The method of claim 6, wherein:

the organism is a canine; and

a single administration of the composition provides the following amounts of benzimidazole, avermectin, and praziquantel to the canine:

about 100 mg fenbendazole per kg body weight,

about 0.006 mg ivermectin per kg body weight, and

about 5 mg praziquantel per kg body weight.

20. The method of claim 6, wherein:

the organism is a canine, and

the canine is treated against an *Ancylostoma caninum and/or Trichuris vulpis* infection.

US 20080075759A1

(19) **United States**

(12) **Patent Application Publication** (10) **Pub. No.: US 2008/0075759 A1**

Paulsen et al. (43) **Pub. Date: Mar. 27, 2008**

(54) **PROCESS FOR MANUFACTURING CHEWABLE DOSAGE FORMS FOR DRUG DELIVERY AND PRODUCTS THEREOF**

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(21) Appl. No.: **11/940,106**

(22) Filed: **Nov. 14, 2007**

Related U.S. Application Data

(63) Continuation-in-part of application No. 11/296,181, filed on Dec. 7, 2005.

Publication Classification

(51) **Int. Cl.**
A61K 47/00 (2006.01)

(52) **U.S. Cl.** **424/439**

(57) **ABSTRACT**

A palatable, edible soft chewable medication vehicle for delivery of a pharmaceutically acceptable active ingredient, such as a drug, to an animal or human subject. The edible soft chews contain only food grade or better inactive ingredients, and preferably do not contain ingredients of animal origin. Processes for manufacturing the edible soft chews do not require the use of heat or the addition of water during mixing of active and inactive ingredients, provide stable concentrations of the active ingredient, and produce chews of consistent weight and texture.

PROCESS FOR MANUFACTURING CHEWABLE DOSAGE FORMS FOR DRUG DELIVERY AND PRODUCTS THEREOF

STATEMENT REGARDING RELATED U.S. APPLICATIONS

[0001] This is a continuation-in-part of U.S. patent application Ser. No. 11/296,181, filed Dec. 7, 2005.

FIELD OF THE INVENTION

[0002] The invention relates to the field of orally administrable pharmaceutical dosage units; in particular, units in the form of an edible mass, such as a chunk.

BACKGROUND OF THE INVENTION

[0003] Formulation of a drug into an edible medication, such as a chewable tablet or confection, can increase patient acceptance of the medication, especially animals, who tend to resist swallowing hard tablets or capsules. Unfortunately, many drugs and other active ingredients (collectively, "actives") have a strongly bitter or otherwise unpalatable taste, making chewing them unpleasant.

[0004] Flavorings are commonly added to chewable medications to enhance their palatability. For example, a veterinary medication might include animal product-based flavorings such as uncooked dried meat parts such as beef, pork, chicken, turkey, fish and lamb; organ meats such as liver; meat meals, bone meals and ground bone; and animal-derived food such as casein, milk (which may include dry forms and lowered fat forms, such as dry skim milk), yogurt, gelatin, cheese and egg (collectively, "animal origin flavorings") may be utilized.

[0005] However, use of many animal origin flavorings (especially of meat, poultry or seafood origin) risks exposure to infectious agents, not only to the recipient of the drug, but also through contamination of manufacturing equipment on which the flavored dosage units are made. For this reason, manufacturing facilities that prepare pharmaceutical products with animal origin flavorings are often devoted exclusively to their preparation, at a correspondingly greater cost than would be incurred if manufacturing could be performed in a facility capable of concurrently processing multiple products.

[0006] Texture is also an issue for chewable medications. One of the most commonly used form for chewable dosage units is the compressed tablet, whose ingredients (including the actives and inactive ingredients such as binders) can make the tablet gritty or otherwise unappealing, especially to animals. Thus, a preferred alternative dosage form for use especially with animals is the "edible soft chew," generally a meat-like mass or chunk also widely found in consumable pet treats, having a softness similar to a cooked ground meat patty.

[0007] Edible soft chews are typically manufactured by blending and extrusion. Pre-mixed ingredients are introduced into an extruder barrel with a screw therein, then mixed, coagulated, expanded and sheared into a blended mixture, followed by application of additional heat if a harder texture is desired, or water has been introduced into the mixture. Water introduced into the mixture must generally be of pharmaceutical grade, as it will be retained within the mixture. The blended mixture is then formed into a desired shape on a die plate, then cut into individual units.

[0008] The heat generated during the extrusion process can cause deterioration in the stability (potency or integrity) of the active in the mixture, causing the effective dose provided by each unit formed to vary. In particular, the heat from compression exerted during extrusion, especially auger extrusion can exceed the melting point of many compounds. Consistency of texture, shape and weights of the chews from batch to batch of extruded material can also suffer.

[0009] There is a need, therefore, for a method of manufacture for edible soft chewable medications in which the blending of actives into the chew mixture is achieved without generation of heat at a level that would cause the active to wholly or partially degrade. Preferably, the method would be performed without application of any heat above room temperature to the mixture or formed product. It is also desirable that the chews be susceptible to manufacture without use of costly, pharmaceutical grade water as an ingredient. There is also a need in the art for a edible soft chew medication whose taste appeals to animals without use of ingredients that may include infectious agents or contaminants. Further, it is highly desirable for the manufacturing means employed to produce chewable medications to do so in a manner that ensures consistent chew weights, texture and active dosages.

SUMMARY OF THE INVENTION

[0010] The invention provides a unique edible soft chew dosage form medication and processes for its manufacture. The edible soft chews of the invention are particularly palatable to pet animals. They contain inactive ingredients of at least food grade quality, and most preferably do not contain inactive ingredients of animal origin. As such, the edible soft chews may be manufactured without concern about transmission of infectious agents or contaminants, and without risk of cross-contaminating other products produced in the same manufacturing facility.

[0011] The manufacturing processes of the invention allow the edible soft chews to be produced wherein the blending of actives into the chew mixture is achieved without generation of heat at a level that would cause the active to wholly or partially degrade. The method is performed so the chew mixture and formed chews are not exposed to temperatures at or above those typically generated by compression and/or shear stress exerted in extrusion, which may be measured by means known to those of ordinary skill in the manufacturing arts (see, e.g., Vermeulen et al., *Chemical Engineering Science* (1971) 26: 1445-1455; Chung et al., *Polymer Engineering and Science* (1977) 17: 9-20; Mount et al., *Polymer Engineering and Science* (1982) 22(12): 729-737; Lindt, J. T., *Conference Proceedings, ANTEC '84, Society of Plastics Engineers* (1984) 73-76; Rauwendaal, C., *Conference Proceedings, ANTEC '93, Society of Plastics Engineers* (1993) 2232-2237; Miller et al., *Conference Proceedings, ANTEC '74, Society of Plastics Engineers* (1974) 243-246; Derezinski, S. J., *Conference Proceedings, ANTEC '88, Society of Plastics Engineers* (1988) 105-108; Derezinski, S. J., *Journal of Materials Processing & Manufacturing Science* (1997) 6(1): 71-77; Derezinski, S. J., *Conference Proceedings, ANTEC '96, Society of Plastics Engineers* (1996) 417-421).

[0012] Preferably, the chew mixture and formed chews are not exposed to temperatures of more than about 10° above room temperature (20° C.), may be exposed to temperatures as low as 0° to about 10° below room temperature, and most preferably are maintained at room temperature throughout the blending and forming steps. As such, the actives in the chew mixture and formed chews are not exposed to heats above or below the temperatures stated during performance of the blending and forming steps, whether by admixture with ingredients at temperatures outside the stated ranges, by application of heat generated by a heat source or compression, or by other means. Stability of the actives is therefore preserved during mixing and formation of the edible soft chews, and a well-blended, soft texture is provided.

[0013] No water is used as an ingredient of the chews, thereby avoiding the need for use of costly pharmaceutical grade water, while reducing the opportunity for microbial growth or loss of potency by the active.

[0014] It has also been found that admixture of actives with an oil to form a suspension that is then admixed with the dry ingredients of the chew facilitates uniform distribution of the active in the finished product. Preferably, the active will also be coated to conserve the potency of the active prior to admixture with the oil.

[0015] For the blending of the coated active suspension with other ingredients of the edible soft chews (e.g., flavorings) a horizontal mixer is preferably used. Such mixers are uniquely well-suited to spins the chew mixture into particulate form. The mixing action causes the ingredients in the mixture to be cast away from the mixing vessel walls, crisscrossing the vessel to provide a uniformly blended mixture formed without application of heat. Because no cooling step is required, the time to produce chews is shortened compared to cooking extrusion methods.

[0016] The highly blended mixture produced is placed into molds without extrusion and formed into individual dosage units that are allowed to set without application of heat. Edible soft chews can be produced in any desired shape. Preferred mixing and molding equipment utilized in the invention can provide individual edible soft chews with consistently blended ingredients, stably provided actives and consistent weights.

[0017] The edible soft chews of the invention are produced in palatable form without the use of any non-food grade inactive ingredients (or, preferably, any animal origin inactive ingredients). The manufacturing processes may therefore be performed without risk of potential cross-contamination of other equipment in the facility with infectious agents or contaminants derived from sources such as the animal-origin meat flavorings commonly used in chewable medications for animals.

DETAILED DESCRIPTION OF THE INVENTION

A. Materials For Use In Edible Soft Chews of the Invention.

[0018] In general, edible soft chewable medications and treats include as inactive ingredients matter such as binding agents, vitamins, and colors to enhance the manufacturability, texture and appearance of the product. Those of ordinary skill in the art will be familiar with such inactive ingredients, which need not include water for use in the invention. No inedible ingredients are present within the soft chews.

[0019] For use in the invention, no inactive ingredients of the edible soft chew should be of less than food grade quality and may be of higher quality (e.g., USP or NF grade). In this context, "food grade" refers to material that does not contain or impart chemicals or agents hazardous to health. Thus, a food grade flavoring, if of animal origin, will be one that has been prepared to substantially reduce or eliminate the presence of infectious agents or contaminants therein; e.g., by processes such as pasteurization, pressurization or irradiation.

[0020] The latter process in particular can effectively eliminate infectious agents such as *E. coli* O157:H7, *Salmonella* and *Campylobacter* from a wide variety of food and animal-derived substances, such as raw meat products, vegetables, grains and fruits. Preferably, however, edible soft chews of the invention will not contain any animal origin ingredients, and most preferably will not contain any animal origin flavorings. All ingredients should be pharmaceutically acceptable (e.g., food grade, USP or NF, as appropriate).

[0021] Flavorings are preferably present in edible soft chews of the invention that are at least food grade in quality, and most preferably exclude animal origin flavorings. Preferred non-animal origin flavorings are plant proteins, such as soy protein, to which edible artificial food-like flavorings has been added (e.g., soy-derived bacon flavoring). Depending on the target animal, other non-animal flavorings could include anise oil, carob, peanuts, fruit flavors, sweeteners such as honey, sugar, maple syrup and fructose, herbs such as parsley, celery leaves, peppermint, spearmint, garlic, or combinations thereof.

[0022] A particularly preferred flavoring for use in the invention is Provesta™ 356, made by Ohly, Inc. It is a light tan, water-soluble powder that builds on the properties of yeast extracts and reaction flavors to provide a pleasant smoky, cured bacon flavor. Provesta 356 contains no animal derived ingredients.

[0023] For administration to horses and other grazing animals, as well as small animals such as rabbits, hamsters, gerbils, and guinea pigs, grains and seeds are especially appealing additional flavoring agents. The grains may be present in any form consistent with the production of the chew including flour, bran, cereal, fiber, whole grain and meal forms, including gluten meals, and may be rolled, crimped, ground, dehydrated or milled. Minerals may also be added as flavorings, such as salt and other spices. Preferably, the grain utilized is dehydrated, milled or flaked. Vegetables such as dehydrated carrots and seeds such as safflower seeds or milo seeds are especially appealing to small animals and may be included.

[0024] Further, agents which enhance the manufacturability and texture of a edible soft chew may include softening agents (which may be an anti-sticking agent), an anti-caking agent or lubricant, and a humectant or wetting agent. Illustrative examples of lubricants or anti-caking agents which may be used in the invention include magnesium stearate, calcium stearate, solid polyethylene glycols. If melted, the

agents are returned to room temperature +/-10° before admixture with an active, sodium lauryl sulfate, or mixtures thereof. Magnesium stearate is particularly preferred for lubrication and as a component to aid in setting the edible soft chews after molding.

[0025] Humectants illustratively include glycerol and propylene glycol, and wetting agents include cetyl alcohol and glycerol monostearate. Glycerin is a preferred humectant useful in maintaining the softness of the edible soft chew over the shelf life of the product. Glycerin is a clear, colorless, odorless, viscous, hygroscopic liquid.

[0026] An anti-sticking agent, preferably polyethylene glycol and most preferably PEG 3350 (Dow Chemical), will preferably be included in the edible soft chew mixture before molding at a volume of about 1.0% to 3.0% w/w. After molding, the edible soft chews with the added anti-sticking agent will set-up, usually over a period of 8 to 24 hours for PEG 3350. PEG 3350 congeals quickly, softens the chew mixture, and prevents the edible soft chew units from sticking together after molding.

[0027] Softening agents utilized are those which limit density and hardness of the edible soft chew product. Such agents may include polysaccharides and fiber. A polysaccharide may be included in the form of a complex food such as a fruit, a plant starch such as potato or tapioca starch. Polysaccharide may also be provided separately, for example, in the form of chondroitin sulfate or glucosamine HCl.

[0028] Fiber may be also provided as filler or as a bulking agent and to provide or maintain porosity in the edible soft chew. Fibers used to this end may be derived from fruits, grains, legumes, vegetables or seeds, or provided in forms such as wood fiber, paper fiber or cellulose fiber such as powdered cellulose fiber. A particularly preferred such bulking agent for use in the invention is bran, such as oat bran.

[0029] Binders utilized in edible soft chews may be a sticky substance, but will preferably give the edible soft chew product a food-like texture. In general, binders may include molasses, corn syrup, peanut butter, a starch such as potato starch, tapioca starch or corn starch, honey, maple syrup and sugars. Preferred binders for use in edible soft chews of the invention are starches.

[0030] A particularly preferred binder is Starch 1500, a pregelatinized starch made by Colorcon Corporation. Pregelatinized starch is a starch that has been chemically and/or mechanically modified to rupture all or part of the starch granules and so render the starch flowable. It contains 5% of free amylase, 15% of free amylopectin and 80% unmodified starch. The source is from corn.

[0031] Powdered sugar (sucrose) serves well as a sweetener as well as a binder. Sucrose is obtained from either sugar cane or sugar beets. Salt and/or other spices may be added as appropriate, with salt being especially preferred to enhance flavor.

[0032] A preservative such as potassium sorbate, sodium benzoate or calcium propionate may be included in order to retard growth of microorganisms and fungi. Tenox 4 is a combination of BHA and BHT anti-oxidants, made by Eastman Chemicals. It is a preferred and convenient preservation system.

[0033] Vitamins may be provided according to the nutritional requirements of the target animal, and may be provided as an element of oils utilized. Vitamins are also present in various oils that may be added as softening agents; for example, canola oil, corn oil, soybean oil and vegetable oil.

[0034] For formation of an active suspension, as well as a flavor enhancer and softening agent, oils are utilized. Vegetable oils (such as corn, safflower, cottonseed, soybean and olive oils) are especially preferred, with soybean oil being most preferred.

[0035] Excipients that may be utilized include starches, cellulose, or derivatives or mixtures thereof, in amounts ranging, for example, from about 1 to about 60 percent (w/w), preferably from about 2 to about 50 percent, more preferably from about 15 to 50 percent. For example, the excipient may consist of sodium starch glycolate, pregelatinized corn starch (Starch 1500), crospovidone (Polyplasdone XL™, International Specialty Products), and croscarmellose sodium (Ac-Di-Sol™, FMC Corp.), and derivatives thereof.

[0036] Excipients may be used to create a trituration of an active. For example, to create a 10% trituration, 100 grams of the active is combined with 900 grams of an excipient, such as a preferred excipient, Starch 1500. Ideally, a geometric dilution of the active is performed, whereby it is first dissolved in a suitable alcohol solvent; e.g., ethyl alcohol. The dissolved active is then combined with the excipient, and the alcohol allowed to evaporate. This step enables a small amount of active to be comprehensively and evenly mixed throughout the starch. The dry mixture is sifted through a screen mesh, fluidized, and is then preferably coated.

[0037] If a coating is to be provided (to help protect the stability of the active and mask its taste), food grade coatings are preferred, such as an aqueous film coat from Colorcon Corporation sold as OPADRY™. OPADRY is a methylcellulose based product with a plasticizer and pigment. Since the coating is aqueous based, no special handling precautions are required during manufacture of the edible soft chew. However, after administration, the aqueous film coat will start to erode and/or dissolve within minutes when exposed to water or other liquids in the stomach. Therefore, disintegration and dissolution of the edible soft chew should not be delayed after it is administered to the subject.

[0038] Any orally administrable active drug or other biologically active compound may be provided in the edible soft chews of the invention. However, the invention is uniquely well-suited to use with actives that are heat-labile, especially at temperatures in excess of 30° C. Those of ordinary skill in the human and/or veterinary pharmaceutical arts will be entirely familiar with the identity of such actives which may include, without limitation, antibiotics, analgesics, antivirals, antifungals, anthelmetics, endo- and ectoparasticides, hormones and/or derivatives thereof, anti-inflammatories (including non-steroidal anti-inflammatories), steroids, behavior modifiers, vaccines, antacids, laxatives, anticonvulsants, sedatives, tranquilizers, antitussives, antihistamines, decongestants, expectorants, appetite stimulants and suppressants, minerals and vitamins.

[0039] The amounts of each of the components in the final product may be varied considerably, depending upon the

nature of the drug, the weight and condition of the subject treated, and the unit dosage desired. Those of ordinary skill in the art will be able to adjust dosage amounts for particular actives in the edible soft chews in light of the teachings of this disclosure. Generally, however, the active may be provided by range in weight based on the total weight of the composition from about 0.001% to 75% (w/w), more preferably 0.095% to 40%, and most preferably not in excess of 50%. For example, for administration of an anthelmetic to dogs, such as ivermectin for treatment of heartworms (see, Example 1) triturated with starch could be added to comprise 31.2% of the foregoing mixture.

[0040] The formula described for the exemplary product may be easily modified for delivery of actives to other species. For example, equine edible soft chews may be based on the same basic formula, substituting molasses powder, oat bran and apple for the bacon. Flavorings particularly appealing to cats include artificial soy based compounds with a fish-like flavor. Human recipients may prefer sweeter flavorings, such as sugars or molasses.

[0041] The edible soft chews of the invention may be packaged individually for administration and stable storage. Examples of suitable packaging materials include HDPE bottles or foil/foil packaging.

B. Processes for Manufacturing Edible Soft Chews of the Invention

[0042] Active and inactive ingredients for a edible soft chew of the invention are added to a mixing vessel of a horizontal mixer capable of blending the material and casting it against the side of the mixing vessels. This action permits the ingredients to be well and consistently blended without application of heat or addition of pharmaceutical grade water to the mixture.

[0043] Horizontal mixers generally comprise a mixing chamber, an elongated, horizontal mixing shaft which rotates, and a plurality of mixing tools which depend generally perpendicularly from the horizontal shaft to rotate around the inside of the chamber (see, e.g., U.S. Pat. No. 5,735,603, the disclosure of which is incorporated herein by this reference). The mixing tools are configured and dimensioned as required for the mixing process to follow the shape of the chamber walls as rotated for proper mixing of all of material present. Some such mixing chambers are cylindrically shaped, while others are trough-shaped, such as mixers which are commonly referred to in the art as double-arm mixers or ribbon mixers.

[0044] In general, a horizontal mixer will have a horizontal mixing shaft extending out of the chamber at both ends. In a motorized mixer, at one end of the shaft, referred to as the drive end, the shaft is operably coupled to a drive motor for rotating the shaft. At the drive end, the shaft is typically coupled through a bearing structure located between the drive motor and the chamber. The bearing structure provides support of the shaft drive end and also ensures smooth rotation. A separate seal structure is often provided further in along the length of the shaft to seal it against leakage of material into and out of the mixing chamber.

[0045] A particularly preferred mixer for use in the invention used is a plough type ribbon mixer with optional agitating blades, sold under the FXM Series™ trademark by Littleford Day Corporation. A 200 kg capacity blender can be used for commercial scale production, and is capable of producing as little as 50 kg of chew mixture for research scale work. No heat is applied during mixing, and the blended product produced has a consistent weight, ingredient distribution and texture from batch to batch.

[0046] Preferably, dry ingredients of the chew mixture are blended first, then an oil suspension of the active blended therein, followed by admixture with the liquid ingredients (e.g., humectants and softening agents) to form a thoroughly blended mixture. After blending, the chew mixture is discharged without compression from a port through the blender into a suitable container for processing into individual dosage units with a forming machine.

[0047] A variety of forming equipment may be utilized in the invention, but those particularly preferred for use are molding machines developed for use in producing molded food products, such as pre-formed hamburger patties and chicken nuggets. For example, the molding machines disclosed in U.S. Pat. Nos. 3,486,186; 3,887,964; 3,952,478; 4,054,967; 4,097,961; 4,182,003; 4,334,339; 4,338,702; 4,343,068; 4,356,595; 4,372,008; 4,535,505; 4,597,135; 4,608,731; 4,622,717; 4,697,308; 4,768,941; 4,780,931; 4,818,446; 4,821,376; 4,872,241; 4,975,039; 4,996,743; 5,021,025; 5,022,888; 5,655,436; and 5,980,228 (the disclosures of which are incorporated herein) are representative of forming equipment that may be utilized in the invention.

[0048] Preferred forming equipment for use in the invention are molding machines that do not apply compression heat to the chew mixture, such as the Formax F6™ molding machine made by the Formax Corporation. The F6 machine has the capabilities of 60 stokes per minute. A square forming die of 6" by 6" can be used to form approximately 16 chunk-like edible soft chew units per stroke, each unit weighing 4 grams and being approximately ⅝" by ⅝" in size. Dies for production of other shapes (e.g., bone shaped chews) may also be utilized.

[0049] In such a machine, a rotary valve opens to cause the chew mixture to flow through fill slots beneath into a first set of mold cavities. A mold plate is advanced, forcing the chew mixture into a second set of cavities, then the mold plate is retracted so the cycle can begin again. The molding mechanism is hydraulic, and works by light pressure on the molding plate, without application of heat.

[0050] A knockout mechanism is provided with cups that align with the cavities to eject molded mixture from all the mold plate cavities simultaneously. For molding edible soft chews of the invention, such a machine could produce an output per hour of approximately 57,600 units, assuming use of a blender mixture yielding 50,000 units per sub batch. Each batch of chews may be packaged in bulk or, preferably, each chew is then individually packaged for storage.

[0051] The invention having been fully described, its practice is illustrated by the examples provided below. Standard abbreviations and measurements apply throughout the examples unless a contrary definition is given. The examples do not limit the scope of the invention, which is defined entirely by the appended claims.

EXAMPLE 1

Edible Soft Chew Formulation

[0052] An example of a edible soft chew suitable for delivery of an active is set forth in Formula 1 below.

Formula 1:

Concentration % w/w	Ingredient
44.69	Starch 1500, USP
19.0	Bacon Flavor (Provesta™ 356), Food Grade
2.0	Polyethylene glycol 3350
20.0	Glycenn, USP
7.0	Vegetable Oil (soybean), USP
0.1	Tenox 4, Food Grade
1.0	Magnesium Stearate, USP
1.0	Yeast Flavoring
5.0	Croscarmellose, sodium N.F.
0.2	Sodium lauryl sulfate
0.001	FD&C Carmine Dye

EXAMPLE 2

Method for Coating Active Ingredients of Edible Soft Chews of the Invention

[0053] A 10% trituration of active (ivermectin) was made by dissolving 100 grams of ivermectin into ethyl alcohol, then mixing the active in 900 grams of Starch 1500 for 3 to 5 minutes. The resultant trituration was allowed to stand until dry, then milled and screened through a 20 mesh screen. The screened trituration was fluidized in a fluidized bed column. A food grade coating (OPADRY™) was applied to the triturated active using a Wurster coater, A top spray fluidized coater, or other suitable device, could also be used for this step. The coated active was then admixed in soybean oil to form a suspension.

EXAMPLE 3

Exemplary Method of Manufacture for Edible Soft Chews of the Invention

[0054] All dry ingredients listed in Examples 1 and 2 were sifted through a 20 mesh screen, then placed into the mixing vessel of a horizontal mixing blender and mixed for 5 minutes. The glycerin was added slowly followed by the slow addition of the vegetable oil/active suspension, and Tenox 4 which had been added to the oil. The product was mixed for 3 minutes. The PEG 3350 was melted then added relatively quickly to the chew mixture, which was then mixed for an additional minute. The mixture resembled a "cookie dough-like" appearance.

[0055] The mixture was formed into individual chunks using a Formax F6™ molding machine with dies for production of chunk-like shapes, and packaged for storage.

[0056] The invention having been fully described, its scope is defined by the claims appended hereto.

The invention that is claimed is:

1. A process for manufacturing a edible soft chewable medication vehicle, the method comprising:

(a) forming an active suspension comprising a coated medicament comprising an active agent and an oil, wherein the medication active is one whose stability or potency can be adversely affected by temperatures typically generated during extrusion;

(b) blending the active suspension formed in step (a) with dry inactive ingredients not of animal origin in a mixer having a mixing chamber and mixing shaft, wherein operation of the mixer causes a edible soft chew mixture to be formed having the active ingredient uniformly blended therein;

(c) adding a water-soluble polyethylene glycol anti-sticking agent to the dry mixture and blending it therein to form a edible soft chewable mixture;

(d) removing the edible soft chewable mixture from the mixer; and,

(e) forming the edible soft chewable mixture into individual unit masses, wherein the unit masses so formed are of consistent weight from unit to unit,

wherein no heat is generated by, or applied during, performance of any step of the method, and wherein further no water is added to the active agent during performance of the method.

2. The process according to claim 1, further comprising the step of preparing a trituration of the active agent with an excipient before the active agent is added to the mixing chamber in step (b).

3. The process according to claim 2, wherein the trituration of the active agent is prepared by a process comprising dissolving the active in an alcohol solvent, mixing the active with the excipient, and allowing the alcohol to dry before adding the triturated active to the mixing chamber.

4. A process for manufacturing a edible soft chewable medication vehicle, the method comprising:

(a) forming an active suspension comprising a coated medicament comprising an active agent active and an oil, wherein the medication active is one whose stability or potency can be adversely affected by temperatures typically generated during extrusion;

(b) blending the active suspension formed in step (a) with dry inactive ingredients not of animal origin in a mixer having a mixing chamber and mixing shaft, wherein operation of the mixer causes a edible soft chew mixture to be formed having the active ingredient uniformly blended therein;

(c) adding a water-soluble polyethylene glycol anti-sticking agent to the dry mixture and blending it therein to form a edible soft chewable mixture;

(d) removing the edible soft chewable mixture from the mixer; and,

(e) forming the edible soft chewable mixture into individual unit masses, wherein the unit masses so formed are of consistent weight from unit to unit,

wherein the edible soft chew mixture and the ingredients thereof are maintained at room temperature or +/−10° C. thereof during performance of any step of the method, and wherein further no water is added to the active agent during performance of the method.

5. The method according to claim 1 or claim 4, wherein the active is one whose potency or stability is adversely affected at temperatures 10° C. over or under room temperature.

6. A medication vehicle in the form of a edible soft chewable mass comprising a medicament, wherein the medication vehicle is produced according to the method of claim 1 or claim 4.

7. The medication vehicle according to claim 6, wherein the medicament is one whose potency or stability is adversely affected at temperatures 10° C. over or under room temperature.

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